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13. ABSTRACT (Maximum 200 Words)

The over-riding hypothesis of this proposal is that muscle tissue, and its major cell type (the myofiber) is an ideal platform on which to test the power of post-genomic research, including integration of DNA, mRNA, and protein data. This tissue is also of considerable importance to the military (muscle function of personnel), and to their families (muscular dystrophy is among the most common of the inherited disorders). An important aspect of post-genomic research is the rapid release of large amounts of data into the public sector, usually via integrated web-accessible databases, typically prior to publication. We have made the first major steps in public access to highly dimensional mRNA data through the construction and implementation of a QC/SOP standardized platform mRNA profile public Oracle web database, currently populated by 887 Affymetrix profiles from human, mouse, and rat. In this current proposal, we request funds for two specific aims. The first is to build upon our experience with our integrated lab mRNA profile Oracle LIMS and Oracle web database, and re-design the structure of the database to enable higher order data analysis tools. This first aim is relevant to the military, as it will provide a national resource for understanding of muscle and nerve function and dysfunction in use, disuse, trauma, regeneration, and dystrophy. The second aim is to extend the integrated data resource from mRNA to protein, using a high throughput ABI TOF/TOF mass spec with comparative proteomics with 18O labeled tryptic digests of protein fractions from normal, atrophic, and dystrophic muscle. This latter aim is also relevant to the military due to the increased understanding of muscle remodeling following specific stimuli that are frequently encountered in the field (loss of weight-bearing following trauma, and plasticity in response to damage).

14. SUBJECT TERMS
Muscular dystrophy, proteomics, genomics, muscle, PEPR

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***INTRODUCTION**: Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

BODY: Following is a re-statement of hypotheses and tasks, and an update on each for the previous 12 months.

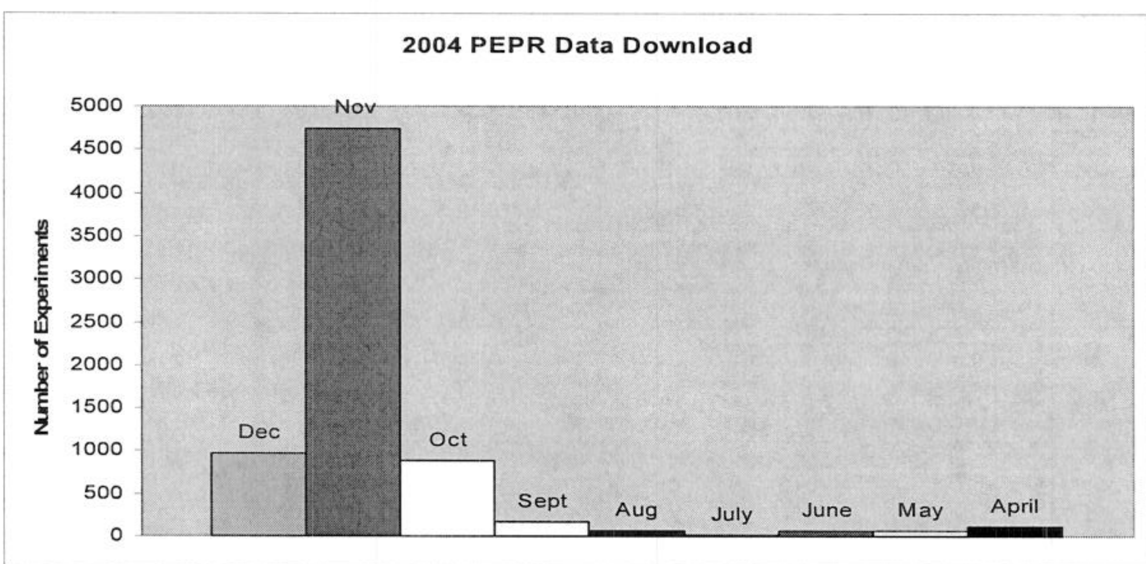
Hypothesis: *Muscle tissue, and its major cell type (the myofiber) is an ideal platform on which to test the power of post-genomic research, including integration of DNA, mRNA, and protein data.*

Task 1. *Create a public access data warehouse for muscle with quality control and standard operating procedures, using a standardized platform, including muscle disease, exercise physiology, and plasticity following muscle damage.*

Aim 1A. Based upon our experience in generating the largest amount of public access vertebrate expression profile data, we will re-design our current integrated internal Oracle LIMS, web Oracle data warehouse, and conversion utilities (NCBI GEO) to reflect changes in GeneChip data structure, web-based query tools, and cross-project comparisons of data. (Year 1).

This Aim has largely been completed as originally proposed, and we have exceeded previous goals in some aspects. As discussed in the original proposal, we had previously implemented a first generation web Oracle database at the http://microarray.cnmcresearch.org site, and had published some initial user analysis tools (see Chen et al. 2004; Appendix 1). We have since finished the complete re-design as described in the proposal, and as detailed more specifically at our new web site database (http://pepr.cnmcresearch.org). This newly implemented database has accomplished all goals as set forth in the original proposal. These are described more fully below.

Perhaps the best indication of usefulness of the public resource is the amount of usage by the public. The user stats are given in the summary section. Here, we show the very recent surge in number of data downloads (number of Affymetrix microarrays). Note that the graph includes only the first week of December, but all of November. From this, it is evident that 4,800 Affymetrix microarrays were downloaded from PEPR in November 2004 alone (the database went live only a few months before, and was not advertised until bugs were worked out). This makes it one of the most active public resources for microarray data.



Aim 1B. Following re-design, the profile data warehouse will be implemented and populated with 50 projects and 1,500 QC/SOP vertebrate expression profiles. (Year 1).

We have exceeded this aim by completing more than 200 projects for about 100 investigators and 50 institutions (Appendix 2). 54 projects containing 1,830 Affymetrix profiles (experiments) have been released to the public, typically prior to publication, via the http://pepr.cnmcresearch.org site. The Appendix also lists all publications emanating from these projects to date.

Aim 1C. A novel data warehouse visualization tool will be implemented on the web site, using the TreeMap visualization program, with functional clusters related to muscle plasticity and disease implemented via simple user interfaces. In this manner, profiles can be quickly studied for "atrophic", "hypertrophic", "dysferlin-deficient", and other gene clusters. This will provide both a novel web-based method for molecular diagnostics, pathway dissection, and identification of active transcript units and functional clusters in any muscle having an "unknown" pathogenesis. (Years 1 and 2).

We have implemented a series of tools on PEPR. First, we have implemented the time series query, as described in the first generation resource (Chen et al. 2004; Appendix 1). Second, we have implemented a new Chart function through integration with NCBI GEO where hierarchical clustering is available. This clustering tool is available for only a subset of projects at this point, but will be extended to the entire database in year 2.

A new interface that we have implemented, but not proposed in the original application, involves the establishment of an SAS server (see http://sas.cnmcresearch.org). This site is not available to the general public yet, but we are proud of the utilities and advantages of this new effort. We have implemented both a very large spinal cord injury data set (5 time points after four types of injury, with profiles at, above, and below the site of injury; approximately 300 profiles visualized), and a 130 biopsy muscular dystrophy dataset. This interface allows very fast dynamic queries of biochemical pathways, individual genes or probe sets, or lists of genes (all implemented in the muscular dystrophy data set; only single gene query in spinal cord data set). An effort in year 2 will be to implement all public projects during year 2, and include gene ontology and biochemical pathway queries. These will include the "atrophic", "hypertrophic" and other "response clusters", as noted in the original aims.

Summary of Deliverables for Aim 1, year 1.

- **PEPR (Public Expression Profiling Resource):** Completed at http://pepr.cnmcresearch.org .
- 547 Java Classes
- 164 jsp pages
- Additional graphical gene query analysis features (GEO Clustering, log/linear, abs/normalized, actual time point/evenly distributed)
- Logging feature
- LIMS/PEPR synchronization
- Proposal submission process
- Remote Affymetrix data submission

Goals for year 2. Enable remote user uploading of data into PEPR.

- **Web analysis tools:** Time series and GEO clustering enabled as originally proposed.

Goals for year 2. Implement the SAS server interface for 20 muscle- and spinal-cord injury related projects, and integrate into PEPR.

Increased public access and data downloads: 4,800 profiles downloaded in November 2004; 225 registered users.

Task 2. *Define the molecular remodeling of the myofiber following two specific conditions known to damage muscle in humans; an atrophic stimulus (disuse following injury, denervation), and regeneration following injury. The injury model used involves "compensatory" changes that prevent further damage to the muscle; these compensatory remodeling events will be defined.*

Specific Aim 2a. *Atrophic stimuli induce a series of active ubiquitination pathways, and the protein targets of the atrophic-specific SCF-complex (atrogin, muscle ring protein) can be identified by normal water and O^{18} water–based tryptic digestions of control and atrophic muscle, screening defined fractions (myofibrillar, cytosolic, membrane) for ubiquitination products. (Year 1).*

We have successfully implemented proteomic profiling in the laboratory, although the "base technique" has changed from O^{18} water–based tryptic digestions to C^{13}-metabolic labeling comparative methods. This change was initiated due to our following preliminary results during the initial funding period:

- O^{18} water–based tryptic digestions were found to suffer from inefficiency of the reactions, making comparative proteomics less quantitative than needed.
- We hired a junior faculty member, Yetrib Hathout, who had more experience and success with the C^{13}-metabolic labeling comparative methods.

For the atrophic stimuli and measurements of ubiquitination pathways, the switch in methodology also required a switch in experimental approach from in vivo to in vitro. Briefly, metabolic labeling is done only in tissue culture conditions, where a sample with all lysines and arginines replaced by a stable isotope is compared to a control culture. We have spent the initial year implementing these new methods, and in year 2 will conduct both 2D and shotgun proteomic profiling after stimulation of the atrophic pathway by serum deprivation or glucocorticoid administration.

Summary of Deliverables for Aim 2, year 1.

Establishment of proteomic profiling methodologies: A series of successful proteomic profiling experiments using metabolic labeling of cultured cells has been completed, with a manuscript submitted for publication and under revision.

We have acquired 4 gigabytes of shot gun (Finnigan LTQ electrospray) data from one experiment, and are beginning to develop the bio-informatics methods to both provide automated analyses of this high throughput profiling data, and develop methods for integration into our PEPR web database.

Goals for year 2. *Develop bio-informatics methods for automated analyses of high throughput shot gun proteomic profiling of metabolic labeling experiments. Conduct an experiment of glucocorticoid response to induce the atrogin-1 ubiquitin ligase pathway, and identify ubiqutinated targets.*

Additional complementary grant sources received: The preliminary data generated under the auspices of this grant allowed us to apply for a national Core center for proteomics of premature birth in an NIH network. We have won this competition. Also, the issue of corticosteroids and denervation initiating the ubiquitin ligation pathway has been expanded in the context of FY05 DoD funding, and has been approved for funding.

Specific Aim 2b. *Dystrophin-deficient mdx mouse muscle shows normal histopathology until 3-4 wks of age, whereupon large-scale necrosis ensures, followed by effective remodeling commensurate with decreased sensitivity to dystrophin-deficiency. We hypothesize that the proteomic comparisons of membrane proteins in the "pre-necrotic" vs. "effectively regenerated" myofibers will permit identification of the remodeling that desensitizes the myofiber to lack of dystrophin. (Year 2).*

The previous reviewers of the original application felt that this sub aim was "overly ambitious", and CDMRP program personnel requested that we remove this sub aim from the proposal. Thus, no progress is reported on this sub aim.

KEY RESEARCH ACCOMPLISHMENTS: Bulleted list of key research accomplishments emanating from this research.

- **PEPR (Public Expression Profiling Resource):** Completed at http://pepr.cnmcresearch.org .
    - 54 public projects
    - 1830 profiles
    - 226 registered users

- **Web analysis tools:** Time series and GEO clustering enabled as originally proposed.
- **Increased public access and data downloads.**
- **Establishment of proteomic profiling methodologies.**

REPORTABLE OUTCOMES: Provide a list of reportable outcomes that have resulted from this research to include:

http://pepr.cnmcresearch.org

CONCLUSIONS: We have succeeded in surpassing the originally proposed Aim 1, with the implementation and use of an advanced web Oracle public access database of QC/SOP Affymetrix microarray expression profiles. Aim 2 on proteomic profiling remains under development, and is to expand in year 2.

REFERENCES: none

APPENDICES:

Appendix 1. Chen et al. 2004

Appendix 2. List of projects and resulting publications.

D578–D581 *Nucleic Acids Research, 2004, Vol. 32, Database issue*
DOI: 10.1093/nar/gkh003

The PEPR GeneChip data warehouse, and implementation of a dynamic time series query tool (SGQT) with graphical interface

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ABSTRACT

Publicly accessible DNA databases (genome browsers) are rapidly accelerating post-genomic research (see http://www.genome.ucsc.edu/), with integrated genomic DNA, gene structure, EST/ splicing and cross-species ortholog data. DNA databases have relatively low dimensionality; the genome is a linear code that anchors all associated data. In contrast, RNA expression and protein databases need to be able to handle very high dimensional data, with time, tissue, cell type and genes, as interrelated variables. The high dimensionality of microarray expression profile data, and the lack of a standard experimental platform have complicated the development of web-accessible databases and analytical tools. We have designed and implemented a public resource of expression profile data containing 1024 human, mouse and rat Affymetrix GeneChip expression profiles, generated in the same laboratory, and subject to the same quality and procedural controls (Public Expression Profiling Resource; PEPR). Our Oracle-based PEPR data warehouse includes a novel time series query analysis tool (SGQT), enabling dynamic generation of graphs and spreadsheets showing the action of any transcript of interest over time. In this report, we demonstrate the utility of this tool using a 27 time point, *in vivo* muscle regeneration series. This data warehouse and associated analysis tools provides access to multidimensional microarray data through web-based interfaces, both for download of all types of raw data for independent analysis, and also for straightforward gene-based queries. Planned implementations of PEPR will include web-based remote entry of projects adhering to quality control and standard operating procedure (QC/SOP) criteria, and automated output of alternative probe set algorithms for each project (see http:// microarray.cnmcresearch.org/pgadatatable.asp).

INTRODUCTION AND DATABASE DESCRIPTION

PEPR provides centralized Affymetrix expression profiling data to the public research community, typically before publication in primary research papers. Data released through PEPR are generated within a single centralized research group (Children's National Medical Center, Microarray Center), with projects originating internally and referred from external institutions. Currently, 1024 Affymetrix arrays representing 38 projects (13 human; 25 mouse/rat) are released to the public. PEPR is an Oracle-based web solution, which permits researchers seamless access to an Affymetrix-only expression profiling database through our web browser without requiring their own Affymetrix software. The web interface also enables users to export many forms of data associated with any particular profile, including raw image files (.dat), processed image files (.cel) and interpretation files (.txt). It allows researchers to perform on-line queries of expression profiles by any number of experimental variables (tissue, species, chip type, etc.). Other built-in functions include searching by GenBank Accession ID and gene name (gene-based cross-profile search). These search functions return signal (Avg Diff) values and Present/Absent Calls (MAS5) for all profiles in PEPR. We also designed and implemented an automated back-end process that disseminates all available PEPR profile data into NCBI Gene Expression Omnibus (GEO) database (http://www.ncbi.nih.gov/geo/) (1). Public users can easily access deposited data in GEO as well as original data files in the PEPR database through a corresponding link created during the direct deposit process.

To our knowledge, the PEPR data warehouse is the largest such public resource adhering to quality control and standard operating procedures (QC/SOP). However, we recognized that the utility of PEPR is dependent on some familiarity with bioinformatics aspects of microarray experiments, where files could be downloaded and analyzed with any method desired.

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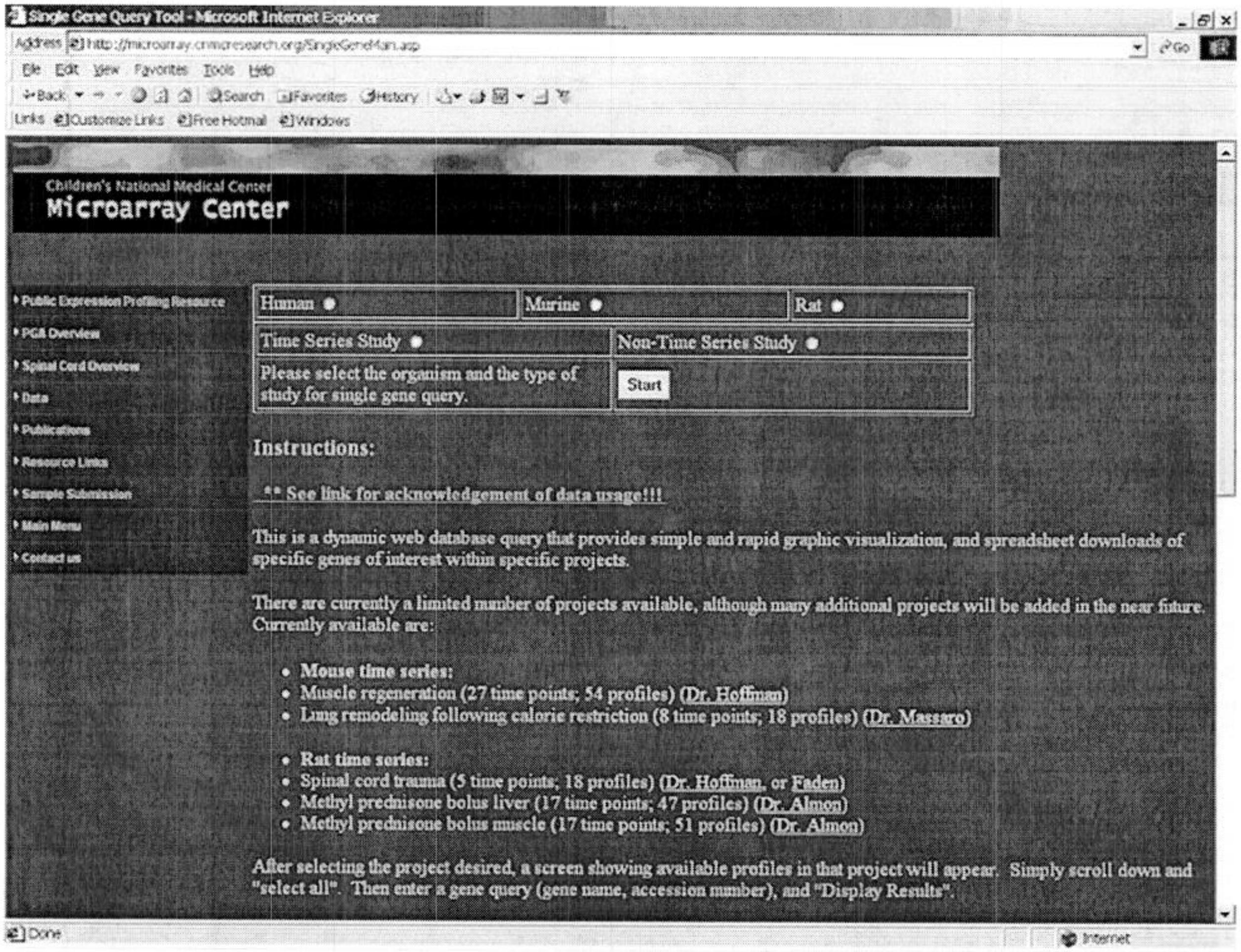

Figure 1. Initial database query for the time series query tool.

To begin to build true user-friendly web-based data analysis tools that do not require experience in formatting and interpretation of microarray data, we designed and implemented a Single Gene Query Tool (SGQT) (see http://microarray.cnmcresearch.org/singlegenemain.asp).

SINGLE GENE QUERY TOOL (SGQT)

Our initial implementation of SGQT is for time series data, which we present here. We provide an entry screen that defines the data subset selections that are available for the user to search (Fig. 1). The specific projects available fitting the search criteria are then presented, and selection of one project leads to a list of all profiles associated with the project. In the example we describe here, a 54 profile, 27 time point muscle regeneration series was selected, with two different muscles profiled at each time point on U74A microarrays containing ~12 000 probe sets (2,3). The user is asked to select the profiles to be studied ('select all' is the option used here to query all 54 profiles). A web browser-style search query is then evoked, and entry of any text or probe set then queries genome databases for all genes and probe sets matching the query. For example, entry of 'myosin' will identify myosin heavy chains, light chains, binding proteins, etc. The user then selects the desired gene from the pull down result menu. Query of 'myogenin' returns only a single probe set, which, when selected ('submit') then triggers the database query tool. The tool then dynamically extracts data from the .cel files for the myogenin probe set from the 54 profile (12 000 probe sets/profile) data set, including signal (normalized hybridization intensity), and absent/present calls (Affymetrix MAS 5.0 determinations). The tool then aligns all data into a time series, and graphs replicates for each time point (Fig. 2), as well as calculating the average of the replicates, graphing the average, and drawing a graph line through the averages for all time points (Fig. 2). The tool also calculates the average signal for each time point, and the fold-change relative to time 0 (based upon array-normalized intensities) (Fig. 2).

The resulting on-line graph has mouse-overs containing data associated with each data point (time point, signal, present/absent call), and for the arithmetic average (time point, average signal, fold-change relative to time 0) (Fig. 2). The mouse-over shown in Figure 2 is for the arithmetic average of replicates, with the pop-up window indicating the fold-change from time 0. Clicking over any data point links to a series of databases (Unigene, GenBank, LocusLink,

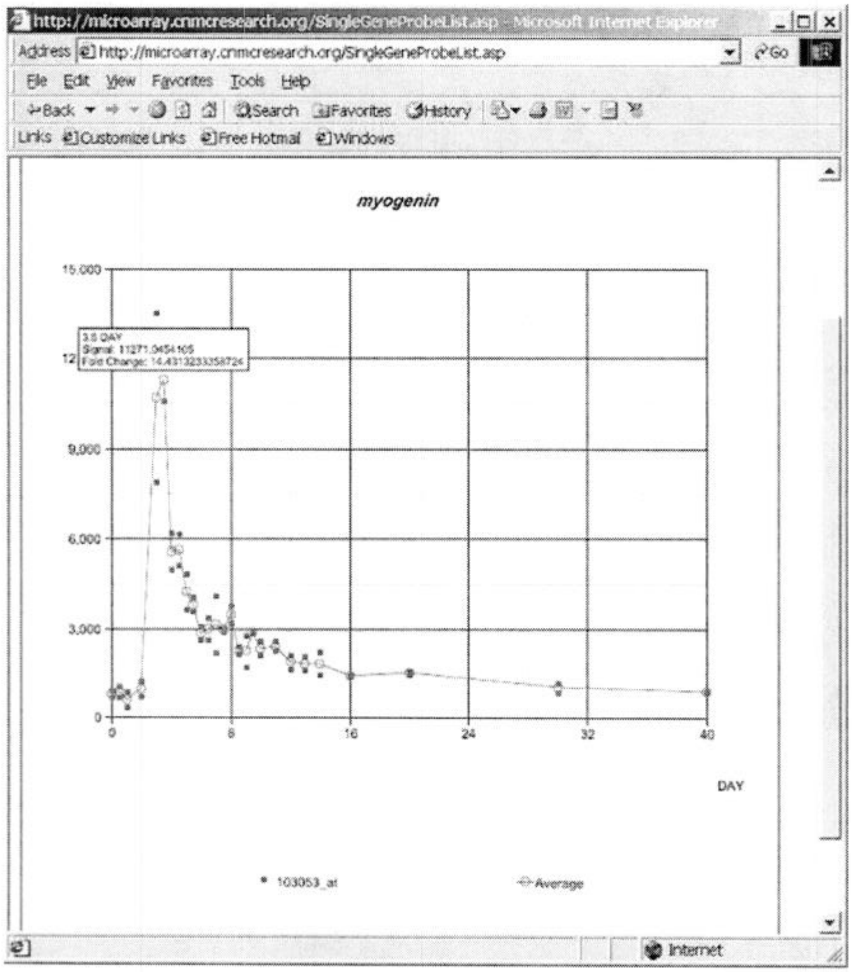

Figure 2. Graphic output of the time series query for myogenin in muscle regeneration. Muscle degeneration/regeneration was induced with intramuscular injection of cardiotoxin, and two different muscles profiled at the indicated time points following injection [see (2) for detailed methods]. Shown is the dynamic database query output of myogenin probe set data contained in 54 U74A Affymetrix microarrays for 27 time points (0–40 days). The green data points are individual expression profiles, with two different muscles profiled and graphed per time point. The purple circle is the average of the replicates, with the graph drawn between the average at each time point. The *y* axis is the relative expression level ('signal') using Affymetrix MAS 5.0. The mouse-over shown corresponds to the average at 3.5 days, and provides both average signal and fold-change relative to time 0 (14.4-fold increase in expression).

Affymetrix) containing information on the gene of interest, as well as access to the download for the original data set (.cel, .dat, or .txt files). The tool also writes a dynamically generated spreadsheet containing all the information in the graph and this appears as a link above the graph. This spreadsheet can be downloaded, and analyzed using any desired graphics or statistical package. It should be emphasized that all visualizations and spreadsheets are dynamic queries of the web Oracle database. The dynamic search and output of the 54 profile murine regeneration series shown here is typically completed in approximately 15 s.

The five time series currently implemented for the tool are a murine *in vivo* 27 time point muscle regeneration series (54 U74A profiles) (2,3), an 8 time point murine lung calorie restriction time series (18 U74A profiles) (4) (D.Massaro and L.B.Clerch, unpublished data), a 5 time point rat spinal cord damage series (18 U34A profiles) (5), and two 17 time point methylprednisone bolus time series in rat (47 profiles in liver and 51 profiles in muscle) (6,7). It is important to note that many experimental variables, such as diurnal variation in gene expression, should be considered when interpreting time series data; for example, in the Massaro and Clerch calorie restriction studies, non-restricted and calorie-restricted mice were killed at the same time. We will continue to add additional time series to the tool, and plan to implement a collection of time series and non-time series data comparisons and visualizations to the PEPR resource.

To our knowledge, the time series query tool described here is the first expression profile data analysis tool that requires no prior knowledge of microarray data format or data interpretation. This tool is useful due to the quality control and replicates available for each time point, and simple visualization, interpretation and download of these. Future implementations of our data warehouse will allow input of externally generated data that conform to minimum experimental design criteria, and our QC/SOP benchmarks (see

http://microarray.cnmcresearch.org/pgaoutline-qcofsamples.asp) via a web interface with automated QC/SOP checks. As PEPR is built upon a standardized platform of Affymetrix-only data adhering to QC/SOP, all internally- and externally-generated data within PEPR should be intrinsically comparable. A new implementation of PEPR including many projects able to be queried by the SGQT tool described here is expected in late 2003. The updated PEPR will also include a choice of probe set algorithm for data display (MAS 5.0, dCHIP, RMA and ProbeProfiler).

MATERIALS AND METHODS

Expression profiling

All expression profiles were generated using total RNA, with *in vitro* transcription yielding biotinylated cRNA for hybridization to Affymetrix GeneChips (see http://microarray.cnmcresearch.org/pgaoutline-qcofsamples.asp). Only one of the 38 projects utilized two-round amplifications from limiting sample (8), and this is clearly indicated in the mouse-over for that project (see http://microarray.cnmcresearch.org/pgadatatable.asp).

Data analysis

We provide .dat, .cel, and .txt interpretation files using Affymetrix MAS 5.0 for all microarrays and projects. Other methods of normalization and probe set interpretation can be used by downloading any desired file types. The single gene query tool uses raw .cel file data, normalized via a common target intensity between all profiles in the project, and provides information on 'present/absent' call determinations, but does not use these for data analysis purposes. We have recently shown that the Affymetrix MAS 5.0 probe set interpretation method provides good signal/noise ratios for expression profiling projects using tissue samples (9).

ACKNOWLEDGEMENTS

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Table Characteristics
Projects: 199
Arrays: 5,550
Principal Investigators: 100
Institutions: 43
Public: 46
References: 58

Project Title	Number of Arrays	PI Last Name	PI First Name	Institution	Is the date public? (PEPR, GEO)	Reference Number
Acolberg Human Cytomegalovirus	9	Colberg-Poley	Anamaris	CNMC Immunology	No	
Acute Quadriplegic Myopathy	32	Hoffman	Eric	CNMC GenMed	Yes	22
ADaluiski Murine Limb Symmetry	12	Daluiski	Aaron	UCLA, Dept of Orthopaedic Surgery	No	54
AFaden Rat Traumatic Brain Inj	51	Faden	Alan	Georgetown University	No	
AHayes Human Neuroblastoma Cell	19	Hayes	Andrea	CNMC Oncology	No	
AKeegan Murine Osteoclast	12	Keegan	Achsah	Holland lab	No	42
AKumar HIV Resistance	5	Kumar	Ajit	George Washington University	No	36
ALL Diagnosis vs Relapse	111	Stephan	Dietrich	CNMC GenMed	No	
ALL Translocations	18	Stephan	Dietrich	CNMC GenMed	No	
alpha Sarcoglycan Deficiency	4	Hoffman	Eric	CNMC GenMed	No	
Avanderver VWM Fibroblast	8	Vanderver	Adeline	CNMC Neurology	No	
BBregman Spinal cord Regeneration	21	Bregman	Barbara	Georgetown University	No	
BPaterson Drosophila Muscle	6	Paterson	Bruce	NIH NCI	No	
Breast Cancer Amplification Chr8q24	2	Stephan	Dietrich	CNMC GenMed	No	
BRood Human HIC1	24	Rood	Brian	CNMC Oncology	No	45
Calcinosis Rider	1	Rider	Lisa	FDA	No	
Calpain 3	5	Hoffman	Eric	CNMC GenMed	No	
CChilders Muscle Dystrophy	8	Childers	Casey	University of Missouri	No	
CLundergan Coronary Restenosis	15	Lundergan	Conor	George Washington University	No	
CNS Regeneration	930	Faden	Alen	Georgetown University	Yes	21
Coronary Artery Disease	2	Hoffman	Eric	CNMC GenMed	No	
Coronary Artery Disease (Indian)	16	Gorospe	Raffy	CNMC GenMed	No	
CStewart Murine EDMD	23	Stewart	Colin	NCI Frederick	No	
DCarper Human Pterygium	6	Carper	Deborah	NIH NEI	No	
DCarper Murine Lens	6	Carper	Deborah	NIH NEI	No	
DMosser Murine Macrophage	10	Mosser	David	University of Maryland	No	
DObrochta Drosophila Transposon	15	Obrochta	David	University of Maryland	No	
DRichards Drosophila Ovary	15	Richards	Dave	Susquehanna University	No	
DStephan ALL COG Project	62	Stephan	Dietrich	CNMC GenMed	No	
DStephan ALL Relapse NonRelapse	37	Stephan	Dietrich	CNMC GenMed	No	
DStephan Alzheimer Brain	22	Stephan	Dietrich	CNMC GenMed	No	
DStephan Australia ALL	22	Stephan	Dietrich	CNMC GenMed	No	
DStephan Murine SSADH	22	Stephan	Dietrich	CNMC GenMed	No	

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Duchenne	95	Hoffman	Eric	CNMC GenMed	Yes	4, 5, 6, 9, 16, 31, 48, 49
Dysferlin Deficiency	16	Hoffman	Eric	CNMC GenMed	No	
EBaehrecke Cell Death	63	Baehrecke	Eric	University of Maryland	No	38
EHoffman Dysferlin Monocyte	4	Hoffman	Eric	CNMC GenMed	No	
EHoffman MDX Treatment	3	Conte-Camerino	Diana	University Bari, Italy	No	
EHoffman MDX Untreated	4	Conte-Camerino	Diana	University Bari, Italy	No	
EHoffman Murine Dystrophy	10	Hoffman	Eric	CNMC GenMed	No	
EHoffman Murine Muscle Denervation	4	Hoffman	Eric	CNMC GenMed	No	
EHoffman Neurodegenerative diseases	30	Hoffman	Eric	CNMC GenMed	No	
Epstein CMV and CAD	18	Epstein	Stephen	Washington Hospital Center	No	10
Epstein Rat Carotid Injury	23	Epstein	Stephen	Washington Hospital Center	No	37
FAhmed Human Glaucoma	4	Tomarev	Stanislav	NIH NEI	No	
FAhmed Murine Glaucoma	36	Tomarev	Stanislav	NIH NEI	No	
Fahmed/DStephan Rat glaucoma	0	Tomarev	Stanislav	NIH NEI	No	1
FBooth MDX	30	Booth	Frank	University of Missouri	Yes	50
FKashanchi Human HeLa Cells	36	Kashanchi	Fatah	George Washington University	No	19, 20
FKRP deficiency	4	Pegoraro	Elena	University of Padova, Italy	No	
FSHD	75	Winokur	Sara	UC Davis	No	52, 53
GBerry Down Syndrome	4	Berry	Gerry	University of Pennsylvania	No	
Hamilton Rat Exercise	8	Hamilton	Marc	University of Missouri	No	8
Hayward Murine HyperPP	4	Hayward	Lawrence	University of Massachusetts, Worces	No	
Hereditary Spastic Paraparesis	14	Hoffman	Eric	CNMC GenMed	Yes	41
HFine Glioma Diagnostics	5	Fine	Howard	NIH NCI	No	
Human Lymphoblast Schizophrenia	4	Stephan	Dietrich	CNMC GenMed	No	
Human Muscle XL-SMA	6	Baumbach	Lisa	University of Miami	No	
Human Rett Syndrome	3	Naidu	Sakku	Johns Hopkins University	No	18, 33
Human Unknown Dystrophy	121	Hoffman	Eric	CNMC GenMed	No	
ICernak Anadamide Intracerebralventricular Injection	23	Cernak	Ibolja	Georgetown University	No	12
JHoumard Gastric Bypass Surgery	12	Houmard	Joseph	East Carolina University	No	
JMorgan Cell Therapy	6	Morgan	Jenny	Hammersmith Hospital	No	

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JMorgan MDX Drug Therapy	11	Morgan	Jenny	Hammersmith Hospital	No	
JNatale Mouse Strains	9	Natale	JoAnne	CNMC GenMed	No	
JNatale Murine Brain Injury	4	Natale	JoAnne	CNMC GenMed	No	
JNatale Murine Rat Brain Injury	105	Natale	JoAnne	CNMC GenMed	No	44
Karyn Esser Regeneration	12	Esser	Karyn	University of Illinois, Chicago	No	
KCsaky Human Macular Degeneration	40	Csaky	Karl	NIH NEI	No	
KEsser Rat Exercise	52	Esser	Karyn	University of Illinois, Chicago	Yes	15
KMPeterson Human Glioblastoma	20	McDonald	Tobey	CNMC Oncology	No	34
KNagaraju Murine Transgenic	4	Kanneboya	Nagaraju	Johns Hopkins University	No	
KPeterson Medulloblastoma	49	Stephan	Dietrich	CNMC GenMed	Yes	39
KRao Human Platelet	30	Rao	Koneti	Hahnemann University	No	
KVandenborne cast	28	Vendanborne	Krista	University of Florida, Gainesville	No	
KVandenborne Spinalcord Injury	6	Vendanborne	Krista	University of Florida, Gainesville	No	
Larson Aging	12	Larson	Lars	Penn State University	No	
LClerch Murine Lung Regeneration	9	Clerch	Linda	Georgetown University	No	18, 40
Leukodystrophy	2	Gorospe	Raffy	CNMC GenMed	No	
Llarson Aging muscle	2	Larson	Lars	Penn State University	No	
LWu Drosophila Immunity	33	Wu	Louisa	University of Maryland	No	
Malignant hypothermia	4	Hoffman	Eric	CNMC GenMed	No	
Margaret Sutherland Murine ALS	35	Sutherland	Margaret	George Washington University	No	
MBakay Murine Calpain	15	Spencer	Melissa	UCLA	No	
MBakay Unknown Dystrophies	23	Hoffman	Eric	CNMC GenMed	No	
MBurnett Angiogenesis Human	3	Burnett	Mary	Washington Hospital Center	No	
MBurnett Angiogenesis Murine	36	Burnett	Mary	Washington Hospital Center	No	
MBurnett Angiogenesis Rabbit	2	Burnett	Mary	Washington Hospital Center	No	
MRenni Human Exercise	30	Renni	Mike	University of Scotland, Dundee	No	
MRose Goblet Cell Metaplasia	24	Rose	Mary	CNMC GenMed	No	
Murine Neurofibromatosis	52	Natale	JoAnne	CNMC GenMed	Yes	
Murine Neuron Degeneration ALS SOD	47	Sutherland	Margaret	George Washington University	No	
Murine Occipital Ablation	110	Natale	JoAnne	CNMC GenMed	No	44
Murine Random Primer	10	Stephan	Dietrich	CNMC GenMed	No	
Murine Spasmodic Spinal Cord	18	Hoffman	Eric	CNMC GenMed	No	
Murine Spastic Spinal Cord	8	Hoffman	Eric	CNMC GenMed	No	

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Murine Spinal Cord	2	Hoffman	Eric	CNMC GenMed	No	
Muscle Regeneration	155	Hoffman	Eric	CNMC GenMed	Yes	13, 55, 56, 57, 58
NDiFronzo Murine Leukemia MCF247W	4	DiFronzo	Nancy	CNMC Immunology	No	
Neurodegenerative Diseases	42	Hoffman	Eric	CNMC GenMed	No	
Neuromuscular Junction	48	Hoffman	Eric	CNMC GenMed	No	
NINDS Rat Epilepsy Diet	12	Dingledine	Ray	Emory University	Yes	
NINDS Rat Hippocampus Seizures	35	Koh	Sooky	Northwestern University	Yes	
NINDS Rat Neuron Parkinsons	17	Greene	Jim	Emory University	Yes	
Normal Canine Muscle	9	Chen	Yi-Wen	CNMC GenMed	No	
Normal Human Bone	10	Stephan	Dietrich	CNMC GenMed	No	
Normal Human Brain	22	Hoffman	Eric	CNMC GenMed	No	
Normal Human Cell	9	Stephan	Dietrich	CNMC GenMed	No	
Normal Human Kidney	4	Stephan	Dietrich	CNMC GenMed	No	
Normal Human Liver	3	Stephan	Dietrich	CNMC GenMed	No	
Normal Human Muscle	77	Chen	Yi-Wen	CNMC GenMed	No	
Normal human skin	2	Hoffman	Eric	CNMC GenMed	No	
Normal Human Spleen	3	Stephan	Dietrich	CNMC GenMed	No	
Normal Murine Adipose	2	Garcia	Skip	Johns Hopkins University	No	
Normal Murine Brain	30	Natale	JoAnne	CNMC GenMed	No	
Normal Murine Cell	3	Young	Marian	NIH NIDCR	No	
Normal Murine Heart	2	Hoffman	Eric	CNMC GenMed	No	
Normal Murine Lens	2	Stephan	Dietrich	CNMC GenMed	No	
Normal Murine Liver	4	Hoffman	Eric	CNMC GenMed	No	
Normal Murine Muscle	14	Booth	Frank	University of Missouri	No	
Normal Murine Spinal Cord	23	Hoffman	Eric	CNMC GenMed	No	
Normal Murine Spleen	16	Nagaraju	Kanneboyina	Johns Hopkins University	No	
Normal Murine Trachea	2	Rose	Mary	CNMC GenMed	No	
Normal Rat Eyes	4	Bernstein	Steve	Johns Hopkins University	No	
Normal Rat Muscle	4	Esser	Karyn	University of Illinois, Chicago	Yes	24
Obecher astro cells	24	Becher	Oren	Johns Hopkins University	No	
Pachman Juvenile Dermatomyositis	15	Pachman	Lauren	Chicago Children's	Yes	29, 49

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PClarkson Human Exercise	35	Clarkson	Priscilla	University of Massachusetts, Amhers	No	14
PClarkson SCI Study	6	Clarkson	Priscilla	University of Massachusetts, Amhers	No	
PGA Dog Congestive Heart Failure	5	Hare	Joshua	Johns Hopkins University	Yes	
PGA Human Airway Hyperresponsiveness	33	Scott	Alan	Johns Hopkins University	Yes	
PGA Human Broncial Epithelial	12	Spannhake	E.	Johns Hopkins University	Yes	
PGA Human CD4+ Lymphocytes	140	Diette	Greg	Johns Hopkins University	Yes	
PGA Human Cystic Fibrosis	60	Boyle	Mike	Johns Hopkins University	Yes	
PGA Human Epithelial Cells	6	Scott	Alan	Johns Hopkins University	No	
PGA Human Lung Rejection	9	Garcia	Skip	Johns Hopkins University	No	
PGA Human Lung Tissue	8	Moller	David	Johns Hopkins University	No	
PGA Human Muscle Obese	27	Houmard	Joseph	East Carolina University	Yes	
PGA Human Muscle Statin	32	Clarkson	Priscilla	University of Massachusetts, Amhers	No	
PGA Human Obstructive Pulmonary	10	Rubinstein	Neal	University of Pennsylvania	Yes	
PGA Human Sickle Cell	12	Driscoll	Cathy	CNMC Hematology	No	
PGA Human Systemic Lupus	4	Andrade	Felipe	Instituto Nacional de Cs. Medicas y N	No	
PGA Murine Air Hyperpermability	8	Kleeberger		Johns Hopkins University	Yes	
PGA Murine Airway Hyperresponsiveness	42	Wills-Karp	Marsha	Cinncinnati Children's	Yes	
PGA Murine Alternatively Activated Macrophages (AMM)	5	Scott	Alan	Johns Hopkins University	Yes	
PGA Murine Asthma WKarp	2	Wills-Karp	Marsha	Cinncinnati Children's	No	47
PGA Murine Calories Restriction	52	Massaro	Donald	Georgetown University	Yes	28
PGA Murine Cardiac Hypertrophy	6	Hare	Joshua	Johns Hopkins University	Yes	7, 11
PGA Murine Fibrillin-1 Deficient	30	Neptune	Enid	Johns Hopkins University	Yes	
PGA Murine Glucose Metabolism	19	ODonnell	Chris	Johns Hopkins University	Yes	
PGA Murine Goblet Cells	5	Rose	Mary	CNMC GenMed	Yes	
PGA Murine IL-13 Asthma	26	Wills-Karp	Marsha	Cinncinnati Children's	Yes	
PGA Murine Lung Estrogen	28	Massaro	Donald	Georgetown University	Yes	
PGA Murine Lung Hyperoxia	48	Kleeberger	Steven	Johns Hopkins University	Yes	25
PGA Murine Lung Hypertension	30	Li	Dechun	Johns Hopkins University	Yes	
PGA Murine Lung Ragweed	49	Wills-Karp	Marsha	Cinncinnati Children's	Yes	
PGA Murine Lung Septation	8	Clerch	Linda	Georgetown University	Yes	

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PGA Murine Myotubes Statins	3	Clarkson	Priscilla	University of Massachusetts, Amhers	No	
PGA Murine Pulmonary Fibrosis	39	Moller	David	Johns Hopkins University	Yes	
PGA Rat Kidney Methylprednisolone	74	Almon	Richard	SUNY Buffalo	No	27
PGA Rat Liver Methylprednisolone	47	Almon	Richard	SUNY Buffalo	Yes	32
PGA Rat Lung Seoul	12	Glass	Greg	Johns Hopkins University	Yes	35
PGA Rat Lung Ventilation	9	Pearse	Skip	Johns Hopkins University	Yes	
PGA Rat Muscle Methylprednisolone	53	Almon	Richard	SUNY Buffalo	Yes	2, 51
PGA Rat Necrotizing Enterocolitis	29	Upperman	Jeffrey	University of Pittsburgh	Yes	
PPlotz Human Myositis	12	Plotz	Paul	NIH NIAMS	No	
PRay HIV-Tg-Rat Profiling	28	Ray	Patricio	CNMC Nephrology	No	
PRay Low-K-Study Profiling	13	Ray	Patricio	CNMC Nephrology	No	
PRay Rat Cocaine	2	Ray	Patricio	CNMC Nephrology	No	
PRussell Human Glaucoma	12	Russell	Paul	NIH NEI	Yes	
Rett Syndrome	12	Naidu	Sakku	Johns Hopkins University	No	18, 33
RFreishtat Acute Lung Injury	28	Freishtat	Robert	CNMC GenMed	No	
RGorlick Osteosarcoma Comparison	61	Gorlick	R	Memorial Sloan-Kettering	No	
RGorospe XDP Fibroblast	2	Gorospe	Raphael	CNMC GenMed	No	
RMcKay Stem Cells	32	McKay	Ron	NIH NINDS	No	
RMcKay Stem Cells B	24	McKay	Ron	NIH NINDS	No	
RReeves Murine Trisomy	74	Reeves	Roger	Johns Hopkins University	No	46
SBernstein Rat Retina Stroke Model	17	Bernstein	Steve	Johns Hopkins University	No	
SDutta PCB Metabolism	12	Dutta	Sisir	Howard University	No	
Skeletal Genome Anatomy Proj	23	Stephan	Dietrich	CNMC GenMed	Yes	
SLadisch Human HUVEC Ganglioside	10	Ladisch	Stephan	CNMC Oncology	No	
SLadisch-Human Dendritic Cells	16	Ladisch	Stephan	CNMC Oncology	No	
SPateirno Human Fibroblast	23	Patierno	Steven	George Washington University	No	
SYakovlev Human Cell Apoptosis	12	Yakovlev	Alexander	Georgetown University	No	
Systemic Lupus Erythematosus	55	Andrade	Felipe	Instituto Nacional de Cs. Medicas y N	No	
THaydar Subventricular Zone	2	Haydar	Tarik	CNMC Neuroscience	No	
TMacDonald Human Medulloblastoma (DAOY)	24	MacDonald	Tobey	CNMC Oncology	No	
VGallo Oligodendroglial Profiling	54	Gallo	Victorio	CNMC Neuroscience	No	
VSartorelli Myogenesis MyoD	30	Sartorelli	Vittorio	NIH NIAMS	No	30, 31

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VSartorelli p300	9	Sartorelli	Vittorio	NIH NIAMS	No	
VSartorelli SMC Calorie Restriction	24	Sartorelli	Vittorio	NIH NIAMS	No	40
VSartorelli SMC differentiation	47	Sartorelli	Vittorio	NIH NIAMS	Yes	
WKraus STRRIDE Study	39	Kraus	William	Duke University	Yes	26
WRebeck Alzheimer Neuronal Cell	6	Rebeck	William	Georgetown University	No	
WSilk Macular Degeneration	56	Csaky	Karl	NIH NEI	Yes	
XDChen Osteoblast BGN-KO	7	Young	Marian	NIH NIDCR	No	
YChen Fetus Specific Gene	4	Chen	Yi-Wen	CNMC GenMed	No	
YChen Juvenile Dermatomyositis	66	Pachman	Lauren	Chicago Children's	No	
YChen Murine FSHD	31	Winokur	Sara	UC Davis	No	

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